

## SUBSTITUTE COMBINED DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name; and

I verily believe that I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled: **PEPTIDE NUCLEIC ACID CONJUGATES** the specification of which was filed on <u>October 6, 1995</u> as International Application Serial No. <u>PCT/US95/12931</u>.

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

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| Country        | Number | Date Filed          | Priority Claimed |
|----------------|--------|---------------------|------------------|
| <u>Denmark</u> | 986/91 | May 24, 1991        | Yes              |
| Denmark        | 987/91 | <u>May 24, 1991</u> | <u>Yes</u>       |
| Denmark        | 510/92 | April 15, 1992      | <u>Yes</u>       |

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Status (patented,

Application Serial No. Filing Date

08/275,951

 pending)

 08/319,411
 October 6, 1994
 Pending

 PCT/EP92/01219
 May 22, 1992
 Pending

 (now U.S. Serial No. 08/108,591 filed November 22, 1993)

 08/088,658
 July 2, 1993
 Patented

 08/088,661
 July 2, 1993
 Pending

I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith: John W. Caldwell and Michael P. Straher, Registration Nos. 28,937 and 38,325 of the firm of WOODCOCK WASHBURN KURTZ MACKIEWICZ & NORRIS LLP, One Liberty Place - 46th Floor, Philadelphia, Pennsylvania 19103, and Herb Boswell and Laurel Bernstein, Registration Nos. 27,311 and 37,280, of ISIS Pharmaceuticals, Inc., 2292 Faraday Avenue, Carlsbad, California 92008.

July 15, 1994 Pending

Address all telephone calls and correspondence to:

Michael P. Straher

WOODCOCK WASHBURN KURTZ MACKIEWICZ & NORRIS LLP
One Liberty Place - 46th Floor
Philadelphia, PA 19103
Telephone No. 215-568-3100.

|   | Full Name: Peter NIELSEN   | Inventor's Signature:  | Date:      |  |
|---|--|--|------------|--|
| 1 | Residence: Kokkedal, DENMARK                                       | Citizenship: Denmark   |            |  |
|   | Post Office Address: Hjortevanget                                  | 509, DK 2980 Kokkedal, D   | ENMARK     |  |
| 2 | Full Name: Ole BUCHARDT (deceased)                                 | Inventor's Signature:  O'DUCUAL AND T  Signing upon information and belief as the Representative of the Estate of Ole BUCHARDT | Date 5/299 |  |
|   | Residence: Vaerlose, DENMARK                                       | Citizenship: Denmark   |            |  |
|   | Post Office Address: Sondergardsv                                  | ej 73, DK 3500, Vaerlose,  | DENMARK    |  |
| 3 | Full Name:<br>Soren Holst SONNICHSEN                               | Inventor's Signature:  | Date       |  |
|   | Residence: Tastrup, DENMARK  | Citizenship: Denmark   |            |  |
|   | Post Office Address: Gronhojgardsvej 13, DK 2630 Tastrup, DENMARK  |  |            |  |
|   | Full Name: Jesper LOHSE  | Inventor's Signature:  | Date       |  |
| 4 | Residence: Copenhagen N, DENMARK                                   | Citizenship: Denmark   |            |  |
|   | Post Office Address: Staerevej 52                                  | , 2.tv, DK 2400, Copenhag<br>DENMARK   | en N,      |  |
| 5 | Full Name:<br>Michael EGHOLM                                       | Inventor's Signature:  | Date       |  |
|   | Residence: Wayland,<br>Massachusetts                               | Citizenship: Denmark   |            |  |
|   | Post Office Address: 34 Grove Street, Wayland, Massachusetts 01778 |  |            |  |

Full Name: Muthiah MANOHARAN Inventor's Signature: Date: 6 Residence: Carlsbad, California Citizenship: United States Post Office Address: 7634 Reposado Drive, Carlsbad, California Full Name: John KIELY Inventor's Signature: Date 7 Residence: San Diego, California | Citizenship: United States Post Office Address: 4230 Corte Facil, San Diego, California 92130 Full Name: Michael GRIFFITH Inventor's Signature: Date 8 Residence: San Diego, California | Citizenship: United States Post Office Address: 5676 Greenshade Road, San Diego, California 92121 Full Name: Kelly SPRANKLE Inventor's Signature: Date 9 Residence: Vista, California Citizenship: United States Post Office Address: 920 Sycamore Avenue, Apt. 61, Vista, California 92083 Full Name: Inventor's Signature: Date Citizenship: Residence: Post Office Address:

PATENT



#### ATION AND POWER OF ATTORNEY SUBSTITUTE COMBINED

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Application Serial No. Filing Date Status (patented, pending)

| 08/319,411                                 | October 6, 1994                            | Pending                  |
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| PCT/EP92/01219<br>(now U.S. Serial No. 08/ | <u>May 22, 1992</u><br>108,591 filed Novem | Pending<br>ber 22, 1993) |
| 08/088,658                                 | July 2, 1993                               | Patented                 |
| 08/088,661                                 | July 2, 1993                               | Pending                  |
| 08/275,951                                 | July 15, 1994                              | Pending                  |

I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith: John W. Caldwell and Michael P. Straher, Registration Nos. 28,937 and 38,325 of the firm of WOODCOCK WASHBURN KURTZ MACKIEWICZ & NORRIS LLP, One Liberty Place - 46th Floor, Philadelphia, Pennsylvania 19103, and Herb Boswell and Laurel Bernstein, Registration Nos. 27,311 and 37,280, of ISIS Pharmaceuticals, Inc., 2292 Faraday Avenue, Carlsbad, California 92008.

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|   | Full Name:<br>Ole BUCHARDT (deceased)   | Inventor's Signature:   | Date    |  |
| 2 |   | Mrs. Dorte BUCHARDT Signing upon information and belief as the Representative of the Estate of Ole BUCHARDT |         |  |
|   | Residence: Vaerlose, DENMARK  | Citizenship: Denmark  |         |  |
|   | Post Office Address: Sondergardsv   | ej 73, DK 3500, Vaerlose,   | DENMARK |  |
| 3 | Full Name:<br>Soren Holst SONNICHSEN  | Inventor's Signature:   | Date    |  |
|   | Residence: Tastrup, DENMARK   | Citizenship: Denmark  | ·       |  |
|   | Post Office Address: Gronhojgardsvej 13, DK 2630 Tastrup, DENMARK               |   |         |  |
|   | Full Name: Jesper LOHSE   | Inventor's Signature:   | Date    |  |
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|   | Post Office Address: Staerevej 52   | , 2.tv, DK 2400, Copenhag<br>DENMARK  | en N,   |  |
| 5 | Full Name:<br>Michael EGHOLM  | Inventor's Signature:   | Date    |  |
|   | Residence: Lexington, Massachusetts   | Citizenship: Denmark  |         |  |
|   | Post Office Address: 1231 Lexington Ridge Drive, Lexington, Massachusetts 02173 |   |         |  |

Inventor's Signature: Date: Full Name: Muthiah MANOHARAN 6 Citizenship: United States Residence: Carlsbad, California Post Office Address: 7634 Reposado Drive, Carlsbad, California Inventor's Signature: Date Full Name: John KIELY 7 Residence: San Diego, California Citizenship: United States Post Office Address: 4230 Corte Facil, San Diego, California 92130 Date Full Name: Michael GRIFFITH Inventor's Signature: 8 Residence: San Diego, California Citizenship: United States Post Office Address: 5676 Greenshade Road, San Diego, California 92121 Full Name: Kelly SPRANKLE Inventor's Signature: Date 9 Citizenship: United States Residence: Vista, California Post Office Address: 920 Sycamore Avenue, Apt. 61, Vista, California 92083 Inventor's Signature: Date Full Name: Citizenship: Residence: Post Office Address:





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| 3 | Soren Holst SONNICHSEN   | South Sonn  | 18/2-99      |  |
| · | Residence: Tastrup, DENMARK  | Citizenship: Denmark  |              |  |
|   | Post Office Address: Gronhojgards                                  | vej 13, DK 2630 Tastrup,  | DENMARK      |  |
|   | Full Name: Jesper LOHSE  | Inventor's Signature:   | Date 22/2 99 |  |
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| 5 | Full Name:<br>Michael EGHOLM                                       | Inventor's Signature:   | Date         |  |
|   | Residence: Wayland,<br>Massachusetts                               | Citizenship: Denmark  |              |  |
|   | Post Office Address: 34 Grove Street, Wayland, Massachusetts 01778 |   |              |  |
|   |  |   |              |  |

Inventor's Signature: Date: Full Name: Muthiah MANOHARAN 6 Citizenship: United States Residence: Carlsbad, California Post Office Address: 7634 Reposado Drive, Carlsbad, California Inventor's Signature: Date Full Name: John KIELY 7 Residence: San Diego, California | Citizenship: United States Post Office Address: 4230 Corte Facil, San Diego, California 92130 Inventor's Signature: Date -Full Name: Michael GRIFFITH 8 Residence: San Diego, California | Citizenship: United States Post Office Address: 5676 Greenshade Road, San Diego, California Full Name: Kelly SPRANKLE Inventor's Signature: Date 9 Citizenship: United States Residence: Vista, California Post Office Address: 920 Sycamore Avenue, Apt. 61, Vista, California 92083 Inventor's Signature: Date Full Name: Citizenship: Residence: Post Office Address:



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| 2           | Full Name:<br>Ole BUCHARDT (deceased)                              | Inventor's Signature:  | Date               |  |
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|             | Post Office Address: Sondergardsv                                  | ej 73, DK 3500, Vaerlose,  | DENMARK            |  |
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| 5           | Full Name: Michael EGHOLM  | Inventor's Signature:  | Date  Jun 29, 1999 |  |
|             | Residence: Wayland, Massachusetts                                  | Citizenship: Denmark   | ,                  |  |
|             | Post Office Address: 34 Grove Street, Wayland, Massachusetts 01778 |  |                    |  |
|             |  |  |                    |  |

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GB 1634

DOCKET NO.: ISIS-2112
PATENT APPLICATION



SERIAL NO.:08/817,067

FILED: April 4, 1997

#### IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

RECEIVED

In re application of:

Nielsen et al.

MAY 0 5 1999

Serial No.: **08/817,067** 

Group Art Unit: 1634 NOS CENTER

Filed: April 4, 1997

Examiner: A. Marschel

For: PEPTIDE NUCLEIC ACID CONJUGATES

I, Michael P. Straher, Registration No. 38,325 certify that this correspondence is being deposited with the U.S. Postal Service as First Class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

On April 28, 1999

Michael P. Straher, Reg. No. 38,325

Assistant Commissioner for Patents, Washington, D.C. 20231

Dear Sir:

# TRANSMITTAL OF SUBSTITUTE COMBINED DECLARATION AND POWER OF ATTORNEY

Transmitted herewith are four (4) executed Substitute

Combined Declaration and Power of Attorney forms in the aboveidentified patent application. The subject application is a U.S.

National Phase filing of International Application S.N.

PCT/US95/12931, filed October 6, 1995, which is referenced in the substitute declarations.

DOCKET NO.: ISIS-2112

PATENT APPLICATION

Applicants are filing the substitute declarations due to a clerical error on the previously filed declarations in which one of the priority applications was listed twice (08/088,658) and

(XX) The Commissioner is hereby authorized to charge payment of any fees associated with this communication or credit any overpayment to Deposit Account No. 23-3050.

This sheet is attached in duplicate.

and another priority application was omitted (08/088,661).

Respectfully submitted,

Michael P. Straher Registration No. 38,325

Date: April 28, 1999

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